Antibiotic treatment of suspected neonatal meningitis

Sir,—The annotation on antibiotic treatment of suspected neonatal meningitis seems to demonstrate that optimal treatment of this thankfully rare disorder is still not clear. 1 The suggested array of antibiotic treatment and combined routes of administration may provide cover against a wide range of organisms, but is such treatment in the best interests of every patient? In a sick hypotensive infant who may already have compromised renal function the combination of aminoglycoside and cephalosporin may exacerbate the problem. To state that ‘Gentamicin should be used primarily to treat the associated septicaemia’ is to imply the idea that gentamicin may be of no use in the treatment of cephalosporins that cephalosporins are incapable of doing this. Is there any evidence to suggest that cefotaxime is ineffective in the treatment of bacteremia in neonates? 1

I am concerned by the conviction of the authors in their management proposals. To begin a paragraph stating ‘there is no doubt in our minds that intraventricular treatment should be used’ and end it with ‘there has been no study of intraventricular treatment . . . and little information on the ventricular drug concentration achieved after systemic treatment alone in dilated ventricles’ is perhaps a little rash in view of the findings of significantly increased mortality after intraventricular treatment in the American study. 2

The conclusion of McCracken and colleagues was that ‘intraventricular therapy cannot be recommended for the routine management of neonatal meningitis caused by Gram negative enteric bacilli’. 3 In the absence of a further randomised multicentre trial it is surely ill advised to recommend the adoption of this invasive and potentially dangerous mode of treatment as the standard treatment in neonatal Gram negative meningitis with ventricular dilatation.

A SHORT INSTITUTE OF CHILD HEALTH, EIGHTY LIVERPOOL CHILDREN HOSPITAL AIDER HEY, EASTERN ROAD, LIVERPOOL L12 2AP


Dr Rennie and Gandy comment:

Thank you for giving us the opportunity to reply to the correspondent regarding editorial. Opinions regarding the benefits of intraventricular treatment in neonatal Gram negative meningitis are likely to continue to differ for some time: our recommendations constitute a practical approach based on the existing evidence. Much of the discussion pertaining to this work has been well rehearsed before, including the fact that only 20 cases were actually neonates suffering from meningitis. The combination of cefotaxime with another drug such as gentamicin was suggested because of the evidence in favour of synergism, the improved outlook in gram-negative meningitis with Gram positive infections and the apparent safety after dual treatment, and to combat the emergence of resistance. The advice of our microbiologists has always been to start treatment with a dual regime to obtain rapid bacterial killing. We use a single agent when the baby is improving and sensitivity results are available. Ceftriaxone monotherapy seems promising in adults and may prove useful in the neonatal population. The route of the dose is precisely the type of complication that led us to suggest transfer of such cases to centres with intensive care facilities.

Dr Tarlo’s suggestion that neonatologists should consider high dose dexemethasone is an interesting one and we are aware of the evidence suggesting a reduction in neurological sequelae in older children, most of whom were suffering from haemophilus infection. 4 The report of dexemethasone treatment in neonatal meningitis is planned. 5 The dose suggested is large and high dose steroid treatment has proved detrimental in shock. The relative safety of hydrocortisone for the neonate with Gram negative meningitis than it has been in the general paediatric population.


When should the coeliac patient have an intestinal biopsy?

Sir,—Gluten challenges and intestinal biopsies are stressful procedures both for coeliac patients and for the doctors dealing with them. While we recognise that the time has...
come to reconsider the 1970 European Society of Paediatric Gastroenterology and Nutrition (ESPGAN) diagnostic criteria for gluten sensitive enteropathy. At the Trieste, May 1987, and recently published. A multicentre study indicates that in Italy the vast majority of diagnoses of gluten sensitive enteropathy (more than 90%) are made in young children who are referred with signs of malabsorption, the antigluten antibody test confirm histological picture of the disease. It is rare to find positive for the antigluten antibody test. At the Trieste conference it was stated that these so called typical cases do not need a gluten challenge and can be readily and definitely diagnosed by a single biopsy specimen showing a flat mucosa at the first work up.

Looking back on our hundreds of biopsies we have noticed that whenever the clinical and laboratory data strongly suggested gluten sensitive enteropathy, we nearly always found a flat mucosa at the first intestinal biopsy. It appears then that the initial biopsy recommended by ESPGAN and retained by the Trieste recommendation is seldom informative as its result is highly predictable in typical patients. In these cases (supported by a positive antigluten antibody test and abnormal intestinal permeability test) we suggest that the initial biopsy is avoided and a six to 12 month period of gluten free diet is commenced (figure).

As the first years of a gluten free diet seem to have an imprinting effect on the long term compliance, we believe that the gluten challenge is, at present, unavoidable in the youngest patients because it demonstrates the persistence of the disease to the patient's family. At the end of a three to six month period of gluten challenge (or less if symptoms develop) a biopsy is highly recommended as the relapse is sometimes evident only at the histological level. This single biopsy will confirm the diagnosis of gluten sensitive enteropathy in most cases. If the mucosa looks normal the patient can be left on a free diet and periodically checked to exclude the possibility of a late response to gluten. In our opinion a short period of gluten ingestion, as we propose, should not expose the patient to significant risks.

The above approach is less invasive than the ESPGAN scheme and fully exploits the diagnostic role of the antigluten antibody test at the first assessment of the patient. We also suggest adding the sugar intestinal permeability test, which has proved to be a reliable screening procedure for gluten sensitive enteropathy. For atypical or late onset cases we agree that an intestinal biopsy is always mandatory during the first diagnostic phase. A conclusive note of caution is needed. It is well known that long term treatment of gluten sensitive enteropathy is often unsatisfactory. This is especially true for patients who have found 'sensitive' doctors who are overenthusiastic in their wish to avoid unpleasant biopsies. So far we have followed the ESPGAN diagnostic criteria for coeliac disease with satisfactory results both for patients and for us. Nevertheless, in the light of the new, non-invasive diagnostic tools, we also agree on the need of revising the ESPGAN recommendations. This attempt should be made with the contribution of experts from several European centres.

C CATASSI
G NATALINI
M OSSINI
I M RATSCHG
G VPPA
P L GIORGI

Department of Paediatrics, University of Ancona, Via Corridoni 11, 60123 Ancona, Italy


Urinary growth hormone excretion

Sir,—The paper by Walker and colleagues on the use of urinary growth hormone excretion as a screening test for growth hormone deficiency is of great interest. Words of caution are needed, however, before universal adoption of this test by paediatricians and general practitioners as already proposed.

Of the two clinical groups studied, one (group 2) consisted of patients with previously diagnosed growth hormone deficiency who had been treated for variable periods with growth hormone. It is therefore highly probable, though not stated in the paper, that the timing of the urinary and serum investigations in this group may vary considerably from a normal population, with the serum investigations at the time of diagnosis preceding the urinary one by months or years. In effect the urinary growth hormone estimation has been estimated retrospectively, which makes it difficult to evaluate its usefulness as a prospective test. Little if anything is known about deterioration of growth hormone secretion with time in patients with growth hormone deficiency, especially if they are on replacement treatment. Such data should not be used in the evaluation of the prospective role of urinary growth hormone excretion as a screening test for growth hormone deficiency.

The two different methods of deriving comparisons between overnight urinary growth hormone excretion and peak serum growth hormone concentration after stimulation makes the value of combining the data to determine a conversion coefficient suspect. In addition, as the authors themselves state, urinary growth hormone excretion is log distributed which invalidates regression analysis. Examination of the figure would suggest that for the subjects who were not growth hormone deficient, if any correlation exists at all it could possibly be negative. There are clearly several factors that may influence urinary growth hormone excretion, and more detailed statistical analysis of the separate groups might have been more informative. The correlation coefficients would of course have been less impressive.

The value of a non-invasive test of growth hormone secretion in children would be immense. Although of considerable promise, the study of Walker and colleagues does not yet justify the general introduction of urinary growth hormone estimations and more validation is necessary to establish the full characteristics of this potentially valuable addition to our range of investigations.

Dr Walker comments:

The value has raised questions on certain aspects of our paper that I would like to comment on.

The purpose of presenting the relationship between overnight urinary growth hormone and peak serum response to conventional provocation tests (fig 4) was purely to demonstrate that this simple urine test is as good as the currently available blood tests in identifying those children whose growth problems are due to a relative deficiency of growth hormone. Using all those studies prospectively the relationship between the log transformed urinary growth hormone concentrations and peak serum response to provocation holds (r=0.65, p<0.001) and according to advice from our statisticians is quite valid. To undertake 'a more detailed statistical analysis' would attach far too great a significance to this relationship especially with the controversy surrounding the interpretation of provocation tests.

The data that best evaluates the role of urinary growth hormone excretion as a screening test for growth hormone deficiency in the batch of low serum growth hormone concentrations in response to provocation but a normal urinary growth hormone. Such is our experience and confidence in the method. It is now the first line screen for growth hormone deficiency and offer it as part of our regional endocrine service to Wessex paediatricians.